Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix

Table of Contents

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to the study development at their sites, data collection and development of the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

Declaration of interests

The authors have no competing interests to declare.

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Results

Italian children (Figure S1) more frequently presented with mild disease as compared to other cohorts. The rates of infection in Italian infants was 39% compared with 11.8-18.1% in China and 15% in the United States (U.S.) cohorts. Despite the reduction of emergency department (ED) volumes during this pandemic, fever in infants remained one of the most common reasons for ED visits, even when associated with minor illnesses. Of note, fever was one of the main criteria to test a patient for COVID-19 infection.

Four patients without a prevalent age distribution (1 neonate, 1 infant, 2 adolescents) had pulse oximetry < 95% (room air) with lung involvement either at time of chest x-ray (CXR) or bedside lung ultrasound (US).

CXR was the imaging technique of choice in all EDs while bedside lung US was used only in those children who were assessed by an expert physician sonographer. In our cohort, bedside lung US was used in 10 (10%) cases (9/10 cases as an alternative to CXR, while in 1 case as an adjunct tool to further evaluate an 11-month old patient with severe COVID-19 disease and negative CXR). In 90% cases, lung US showed sonographic interstitial syndrome.

We had 11 children with lung involvement (diagnosed either via CXR or bedside lung US) and preserved oxygenation, likely due to the early presentation of patients to the ED and the early stages and portion of lung involvement. No patient had subsequent hypoxia due to increased lung involvement either during the ED stay or at the time of admission for patients who were hospitalized.

With regards to the admission rate, we reported a comparatively high rate of admission (cumulative 67%). 29% of patients were admitted either to wait the result of the swab or for safety isolation. 38/100 (38%) of admissions were due to the clinical condition (sign, symptoms) of the patients irrespective of disease severity (as defined by to Dong et al.[4]), with 9/100 (range 9% of all patients, or 13.4% of those admitted due to their clinical conditions) admitted to either the Intensive Care Unit (ICU), SubICU, or Neonatal ICU. Overall, Italian admissions rates are different and greater

than those of the U.S. (5.7% of all patients, or 20% of those for whom hospitalization status was known). The same is seen in the ICU admission rates (0.58% of all patients, or 2.0% of those for whom hospitalization status was known). Of note, 7/9 of the ICU admissions were 4 neonates and 3 infants younger than 2 months of age who were admitted to the Neonatal ICU. Five of them were admitted to the NICU based on patient-centered outcomes, which includes clinical condition (age, signs, symptoms) and respiratory status, rather than the imagine results. This better explains why we only saw 1% severe and 1% critical cases, as defined by the most commonly used classification system.[4] This system is based on the use of Computed Tomography (infrequently used in children), and may overestimate the impact of COVID-9 in children.

With the increase in the number of confirmed cases, EDs must face the challenge to differentiate amongst those patients with suspected COVID-19, with proper allocation of resources and treatments.

Table S1. Epidemiologic Characteristics, Clinical Features, and Outcomes of the Italian Cohort CONFIDENCE, Compared with Other Cohorts

Characteristics	**Italian cohort – CONFIDENCE n=100**	**Lu et al.[3] n=171**	**Dong et al.[4] n=731**	**CDC MMWR[5] n=2572**
Age median (range)	**3.3 (0-17.5)**	**6.7 (1day-15years)**	**7 (n.a.)**	**11 (0-17)**
Age distribution – years (according to Lu et al.[3] and Dong et al.[4])	**n (%)**	**n (%)**	**n (%)**	**n (%)**
<1	40 (40.0)	31 (18.1)	86 (11.8)	398 (15.5)
1-5	15 (15.0)	40 (23.4)	137 (18.7)	n.a.
6-10	21 (21.0)	58 (33.9)	171 (23.4)	n.a.
>10	24 (24.0)	42 (24.6)	337 (46.1)	n.a.
Age distribution – years (according to CDC MMWR[5])				
<1	40 (40.0)	31 (18.1)	86 (11.8)	398 (15.5)
1-4	14 (14.0)	n.a.	n.a.	291 (11.3)
5-9	17 (17.0)	n.a.	n.a.	388 (15.1)
10-14	20 (20.0)	n.a.	n.a.	682 (26.5)
15-17	9 (9.0)	n.a.	n.a.	813 (31.6)
Sex				**2490 (96.8)[α]**

F	43 (43.0)	67 (39.2)	311 (42.5)	1082 (43.4)
M	57 (57.0)	104 (60.8)	420 (57.5)	1408 (56.6)
Coexisting conditions[β]	**27 (27)**	n.a.	n.a.	**80 (23)**[γ]
Chronic lung disease	n.a.	n.a.	n.a.	40 (50)
Cystic Fibrosis	5 (18.5)	n.a.	n.a.	n.a.
Neurological	4 (14.8)	n.a.	n.a.	n.a.
Hematological	4 (14.8)	n.a.	n.a.	n.a.
Syndrome	4 (14.8)	n.a.	n.a.	n.a.
Prematurity	3 (11.2)	n.a.	n.a.	n.a.
Cardiac	2 (7.4)	n.a.	n.a.	25 (31.3)
Immunological	2 (7.4)	n.a.	n.a.	10 (12.5)
Oncological	2 (7.4)	n.a.	n.a.	n.a.
Metabolic disease	1 (3.7)	n.a.	n.a.	n.a.
Exposure				**184 (7.2)**[δ]
Family cluster	45 (45.0)	131 (76.6)	n.a.	168 (91)
Other exposure	48 (48.0)	2 (1.2)	n.a.	16 (9)[ε]
Unknown	7 (7.0)	15 (8.8)	n.a.	0
Signs and Symptoms available	**100 (100)**	**171 (100)**	**0**	**291 (11.3)**
Asymptomatic	21 (21.0)	27 (16.0)	94 (12.9)	1 (1.3)[ζ]
Symptomatic	79 (79.0)	144 (84.0)	637 (87.1)	291 (11.3)

Fever, cough or shortness of breath/respiratory distress[η]		28 (51.8)	n.a.	n.a.	213 (73.2)
	Fever	54 (54.0)	71 (41.5)	n.a.	163 (56)
	≤37.5°C	46 (46.0)	100 (58.5)	n.a.	128 (44)
	37.6–38.0°C	15 (15.0)	16 (9.4)	n.a.	n.a.
	38.1–39.0°C	28 (28.0)	39 (22.8)	n.a.	n.a.
	>39.0°C	11 (11.0)	16 (9.4)	n.a.	n.a.
	Cough	44 (44.0)	83 (48.5)	n.a.	158 (54.3)
	Shortness of breath/respiratory distress[η]	11 (11.0)	n.a.	n.a.	39 (13.4)
Refusal to feed or difficulty feeding		23 (23.0)	n.a.	n.a.	n.a.
Rhinorrhea		22 (22.0)	13 (7.6)	n.a.	21 (7.2)
Drowsiness		11 (11.0)	n.a.	n.a.	n.a.
Respiratory distress [η]		11 (11.0)	n.a.	n.a.	n.a.
Nausea or Vomiting		10 (10.0)	n.a.	n.a.	31 (10.6)
	Nausea	3 (3.0)	n.a.	n.a.	n.a.
	Vomiting	10 (10.0)	n.a.	n.a.	n.a.
Fatigue		9 (9.0)	13 (7.6)	n.a.	n.a.
Diarrhea		9 (9.0)	15 (8.8)	n.a.	37 (12.7)
Dehydration		6 (6.0)	n.a.	n.a.	n.a.

Abdominal Pain	4 (4.0)	n.a.	n.a.	17 (5.8)
Headache	4 (4.0)	n.a.	n.a.	81 (27.8)
Sore throat	4 (4.0)	n.a.	n.a.	71 (24.4)
Skin Rash	3 (3.0)	n.a.	n.a.	n.a.
Oxygen saturation < 92%	1 (1.0)	4 (2.3)	n.a.	n.a.
Cyanosis	1 (1.0)	n.a.	n.a.	n.a.
Apnea	1 (1.0)	n.a.	n.a.	n.a.
Tachypnea on admission$^{\theta}$	n.a.	49 (28.7)	n.a.	n.a.
Tachycardia on admission$^{\lambda}$	n.a.	72 (42.1)	n.a.	n.a.
Respiratory support				
No	91 (91.0)	n.a.	n.a.	n.a.
Yes	9 (9.0)	n.a.	n.a.	n.a.
Low-flow oxygen$^{\mu}$	4 (4.0)	n.a.	n.a.	n.a.
High-flow oxygen$^{\nu}$	3 (3.0)	n.a.	n.a.	n.a.
Non-invasive ventilation	1 (1.0)	n.a.	n.a.	n.a.
Mechanical ventilation	1 (1.0)	3 (1.7)	n.a.	n.a.
Outcome				
Discharged	33 (33.0)	n.a.	n.a.	n.a.
Admitted	67 (67)	n.a.	n.a.	147 (5.7)

Admitted for signs and symptoms irrespective of severity of disease	38 (38.0)	n.a.	n.a.	n.a.
Admitted waiting for swab results	4 (4.0)	n.a.	n.a.	n.a.
Admitted for isolation	25 (25.0)	n.a.	n.a.	n.a.
Survived	100 (100)	170 (99.4)	730 (99.9)	2569 (99.9)
Dead	0	1 (0.6)	1 (0.1)	3 (0.1)

Notes: Percentages may not total 100 because of rounding. CONFIDENCE CorOnavirus iNFection In peDiatric EmergeNCy dEpartments, CDC MMWR Center for Disease Control and Prevention Morbidity Mortality Weekly Report, n.a. not available.

In CDC MMWR[5] cohort data on [α]sex, [γ]coexisting conditions, [δ]exposure to SARS-CoV-2 and [ε]other exposure (including travels), and symptoms and signs were only partially available.

[β]Coexisting conditions. **Neurological** (n): epileptic encephalopathy (2) (one of these patients with tracheostomy was the only child requiring intensive care admission and mechanical ventilation), ventriculo-peritoneal shunt (1), autism (1). **Syndrome** (n): Di George (1), CHARGE coloboma - heart defects - choanal atresia - growth retardation - genital abnormalities - ear abnormalities (1), arthrogryposis (1), undefined syndrome, patient presented with multiple intestinal and genital malformations and chronic renal failure (1). **Cardiac** (n): large ventricular septal defect. Closure procedure performed 19 days before emergency department assessment (1); rheumatic hearth disease (1). **Hematological** (n): favism (1), thrombocytopenia (1), severe anemia (2). **Immunological** (n): ulcerous colitis (1), uveitis and nephritis (1). **Oncological** (n): Wilms tumor (1), extrarenal malignant rhabdoid tumor (1). **Metabolic** (n): propionic acidemia (1). In Dong et al.[4], the total number of 731 includes also a missing patient.

[ζ]Asymptomatic in CDC MMWR report[5]: 53 cases with no fever, cough, or shortness of breath had no symptoms reported, but could not be classified as asymptomatic because of incomplete symptom information. One (1.3%) pediatric patient was reported to be asymptomatic.

[η]Respiratory distress describes signs and symptoms related to breathing problems: cough, increased breathing rate, retractions, nasal flaring, shortness of breath and respiratory sounds (e.g. grunting, wheeze, crackling).

[θ]Tachypnea on admission: Tachypnea refers to a respiratory rate higher than the upper limit of the normal range according to age. The normal ranges of respiratory rate (in breaths per minute) were as follows: 40 to 60 for newborns, 30 to 40 for children from 1 month to 1 year of age, 25 to 30 for those 1 to 3 years of age, 20 to 25 for those 4 to 7 years of age, 18 to 20 for those 8 to 14 years of age, and 12 to 20 for those older than 14 years of age.

[λ]Tachycardia on admission: Tachycardia refers to a pulse rate higher than the upper limit of the normal range according to age. The normal ranges of pulse rate (in beats per minute) were as follows: 120 to 140 for newborns, 110 to 130 for children younger than 1 year of age, 100 to 120 for those 1 to 3 years of age, 80 to 100 for those 4 to 7 years of age, 70 to 90 for those 8 to 14 years of age, and 60 to 70 for those older than 14 years of age.

[μ]Low flow oxygen therapy system consists of a device (including nasal cannula, and non-rebreathing masks) to deliver oxygen (up to 15 L/min) to spontaneously ventilating patients.

[ν]High-flow oxygen (HFO) therapy system consists of a heated, humidified high-flow nasal cannula (HFNC) that delivers oxygen flow greater than 15 L/min. It allows FiO_2 adjustment independently from the flow rate.

Table S2. Description of patients who required respiratory support, Italian cohort CONFIDENCE

Sex	Age	Coexisting condition	T (°C)	ED symptoms	Oxygen saturation % (room air)	Chest X-ray findings	Lung ultrasound	Respiratory support	Classification of disease severity
F	4 months	none	38	cough, rhinorrhea, respiratory distress	96	normal	n.p.	low-flow oxygen	moderate
M	11 months	propionic acidemia	36.3	drowsiness, vomiting, respiratory distress	91	normal	Interstitial syndrome multiple B-lines	low-flow oxygen	severe
F	9 days	none	37.8	drowsiness, feeding difficulty	100	n.p.	n.p.	high-flow oxygen	mild

F	15 years 5 months	thrombocytopenia, frequent respiratory tract infection	38.8	cough, rhinorrhea, respiratory distress	97	patchy and ground-glass-like opacity and interstitial changes in the lungs	n.p.	low flow oxygen	moderate
M	12 years 6 months	autism	36.5	cough, nausea, vomiting, respiratory distress	93	pneumonia	n.p.	high-flow oxygen	moderate
M	8 days	none	38.4	drowsiness, feeding difficulty, dehydration, respiratory distress	94	n.p.	Interstitial syndrome multiple B-lines	low-flow oxygen	moderate
F	6 years 5 months	CHARGE syndrome, epileptic encephalopathy	38.1	feeding difficulty, dehydration	97	patchy and ground-glass-like opacity and	n.p.	high-flow oxygen	moderate

						interstitial changes in the lungs			
M	2 months	Ventricular septal defect	38.2	Cough, feeding difficulty, skin rash	n.a.	ground-glass-like opacity and interstitial changes in the lungs	n.p.	non-invasive ventilation	moderate
M	14 years 5 months	epileptic encephalopathy (tracheotomy)	36.5	cough, fatigue, drowsiness, dehydration, respiratory distress	92	patchy and ground-glass-like opacity and interstitial changes in the lungs	n.p.	mechanical ventilation	critical

Notes: T, temperature; ED, emergency department; CHARGE, coloboma - heart defects - choanal atresia - growth retardation - genital abnormalities - ear abnormalities; n.p., not performed; n.a., not available.

Table S3. Laboratory results of the Italian cohort CONFIDENCE, compared with the cohort of Lu et al.[3]

		Italian cohort – CONFIDENCE n=100	**Lu et al.[3] n=171**
Blood routine (unit; normal range)			
White blood cell count ($\times 10^9$/L; 5.5-12.0) [α]		6.9 (0.3-25.0)	6.8 (5.5-8.2)
	>12.0 n (%)	11 (17.7)	n.a.
	5.5-12.0 n (%)	40 (64.6)	n.a.
	< 5.5 n (%)	11 (17.7)	45 (26.3)
Lymphocyte count ($\times 10^9$/L; 1.2-6.0) [β]		2.1 (0.2-9.9)	2.9 (2.2-4.4)
	Lymphocytopenia n (%)	14 (28.5)	6 (3.5)
Hemoglobin (g/dL; 11.0-14.90) [γ]		12.1 (4.9-15.9)	12.6 (11.8-13.5)
Infection biomarkers (unit; normal range)			
Procalcitonin (pg/ml; 0-50) [δ]		20 (4-71)	50 (40-80)
	<50 n (%)	19 (82.6)	59 (36)
	≥50 n (%)	4 (17.4)	105 (64.0)
Blood biochemistry (unit; normal range)			
Lactate dehydrogenase (U/L; 120-300) [ε]		289 (140-631)	246 (207-305)
	≥300 n (%)	22 (59.5)	n.a.
	<300 n (%)	15 (40.5)	n.a.

Alanine aminotransferase (U/L; 7-45) [ζ]		25.0 (9-62)	15 (11-27)
	<45 n (%)	51 (86.4)	38 (64.4)
	≥45 n (%)	8 (13.6)	21 (35.6)
Aspartate aminotransferase (U/L; 10-50) [η]		30.0 (8-93)	30 (24-42)
	<50 n (%)	39 (79.6)	25 (50)
	≥50 n (%)	10 (20.4)	25 (50)

Notes: CONFIDENCE CorOnavirus iNFection In peDiatric EmergeNCy dEpartments. n.a. not available. For Dong et al.[4] and CDC MMWR[5], laboratory data were not available. Number of patients of CONFIDENCE cohort for whom laboratory results were available: [α]white blood cell count 62; [β]lymphocyte count 57; [γ]hemoglobin 61; [δ]procalcitonin 23 (procalcitonin 164 in Lu et al.[3]); [ε]lactate dehydrogenase 37; [ζ]alanine aminotransferase 59 (percentages of Lu et al.[3] were recalculated using as denominator the number of patients for whom the test was available and not the total number of the cohort as originally reported); [η]aspartate aminotransferase 50 (percentages of Lu et al.[3] were recalculated using as denominator the number of patients for whom the test was available and not the total number of the cohort as originally reported.

Table S4. Radiological features findings of the Italian cohort CONFIDENCE, compared with the cohort of Lu et al.[3]

	Italian cohort - CONFIDENCE	**Lu et al.[3]**
Chest X-ray n (%)	35 (35.0)	n.a.
Interstitial abnormality	14 (40.0)	n.a.
Consolidation	6 (17.1)	n.a.
Pleural effusion	1 (2.9)	n.a.
Normal	15 (42.8)	n.a.
Chest Computed Tomography n (%)	n.p.	
Ground-glass opacity	-	56 (32.7)
Local patchy shadowing	-	32 (18.7)
Bilateral patchy shadowing	-	21 (12.3)
Interstitial abnormality	-	2 (1.2)
Lung Ultrasound n (%)	10 (10.0)	n.a.
Sonographic interstitial syndrome[6]	9 (90)	n.a.
Small sub-pleural consolidations	4 (40.0)	n.a.

Notes: CONFIDENCE CorOnavirus iNFection In peDiatric EmergeNCy dEpartments, n.a. not available, n.p. not performed. For Dong et al.[4] and CDC MMWR[5], imaging findings were not available.

Table S5. Comparison of age distribution per classification of disease's severity between the Italian cohort CONFIDENCE, Lu et al.[3], and Dong et al.[4]

Italian cohort - CONFIDENCE						
Age (year)	**Asymptomatic n (%)**	**Mild n (%)**	**Moderate n (%)**	**Severe n (%)**	**Critical n (%)**	**Total n (%)**
<1	5 (5.0)	26 (26.0)	7 (7.0)	1 (1.0)	0	39 (39.0)
1 – 5	4 (4.0)	11 (11.0)	1 (1.0)	0	0	16 (16.0)
6 - 10	8 (8.0)	7 (7.0)	6 (6.0)	0	0	21 (21.0)
>10	4 (4.0)	14 (14.0)	5 (5.0)	0	1 (1.0)	24 (24.0)
Total	**21 (21.0)**	**58 (58.0)**	**19 (19.0)**	**1 (1.0)**	**1 (1.0)**	**100 (100)**
Lu, et al.[3]						
Age (year)	**Asymptomatic, n (%)**	**Mild, n (%)**	**Moderate, n (%)***	**Severe, n (%)**	**Critical, n (%)**	**Total n (%)**
<1	0	6 (18.2)	25 (22.5)			31 (18.1)
1 – 5	1 (3.7)	12 (36.4)	27 (24.3)			40 (23.4)
6 - 10	14 (51.9)	10 (30.3)	34 (30.6)			58 (33.9)
>10	12 (44.4)	5 (15.2)	25 (22.5)			42 (24.6)
Total	**27 (15.8)**	**33 (19.3)**	**111 (64.9)**	0	0	**171 (100)**
Dong et al.[4]						
Age (year)	**Asymptomatic, n (%)**	**Mild, n (%)**	**Moderate, n (%)**	**Severe, n (%)**	**Critical, n (%)**	**Total n (%)**
<1	n.a.	n.a.	n.a.	n.a.	n.a.	86 (11.8)
1 – 5	n.a.	n.a.	n.a.	n.a.	n.a.	137 (18.7)
6 - 10	n.a.	n.a.	n.a.	n.a.	n.a.	171 (23.4)
>10	n.a.	n.a.	n.a.	n.a.	n.a.	337 (46.1)
Total	**94 (12.9)****	**315 (43.1)****	**300 (41.0)****	**18 (2.5)****	**3 (0.4)****	**731 (100)**

Notes: CONFIDENCE CorOnavirus iNFection In peDiatric EmergeNCy dEpartments, n.a. not available. *in the pneumonia (moderate) group of Lu et al.[3], one patient (10 months old) died and two children of unspecified age required invasive ventilation. According to the disease severity classification of Dong et al.[4], the first patient should be included in the critical group, while the other two patients should be included in the severe group. **data are reported only as cumulative. For CDC MMWR[5], the disease severity classification was not available

Figure S1. Geographical distribution of COVID-19 patients of the Italian Cohort CONFIDENCE

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